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ON

# HOW OUR BONES GROW.

MICROSCOPIC STRUCTURE OF BONE,

Illustrating Prof. Cleland's Paper.

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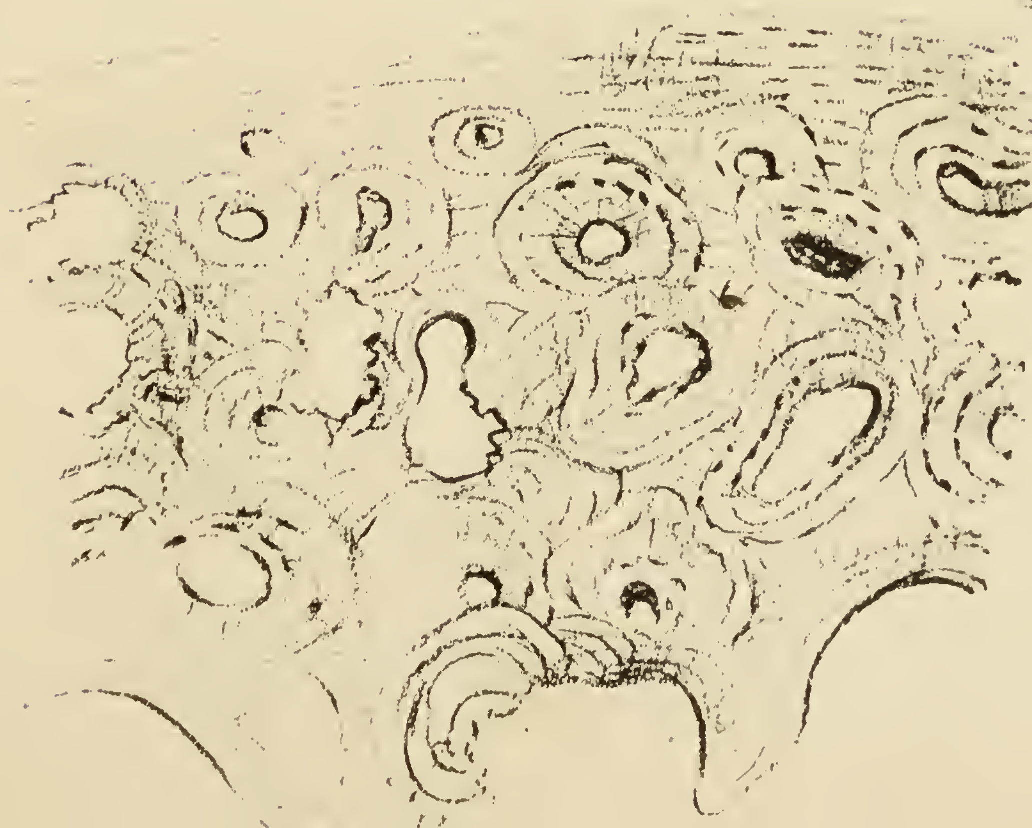

[FROM THE *PROCEEDINGS* OF THE PHILOSOPHICAL SOCIETY OF GLASGOW.]

# *How our Bones Grow.* By JOHN CLELAND, M.D., D.Sc., F.R.S., Professor of Anatomy in the University of Glasgow.

[Read before the Society, 2nd December, 1891.]

GROWTH is a word which includes both increase of bulk and evolution of form. But we do not know in the least what the forces are which lead to the bones or any other part of the body developing the forms which they ultimately assume. I leave that question alone. The growth I have to deal with is not the building of the cathedral, but the manufacture of the bricks of which the cathedral is built. I enquire into the method by which bone increases in bulk, not the agents at work to shape it, so as to take its part in the organism. Now, to understand the growth of bone properly one must begin at the beginning, and recognise that every complex organism, whether vegetable or animal, consists really of a vast colony of minute beings. We are made up of a multitude of microscopic structures which we are in the habit of speaking of as nucleated corpuscles or cells. "Nucleated cells" is, perhaps, the most frequent term. For my own part, I prefer the term corpuscles, because the essential part is not a hollow cell or vesicle, but a mass of protoplasm. These minute masses of protoplasm are living bodies, which in their simplest form are of rounded figure, sometimes throwing out branches in different directions, while in their interior there is a firmer body called a nucleus.

Much more might be said with regard to the composition of such corpuscles, but it is sufficient for you to know that the textures of our bodies all grow through their instrumentality. They all consist either of simple corpuscles, such as I have represented on the slate, or of more complex elements derived from such simple corpuscles, to which in many instances there is added substance deposited between, which is called the stroma or matrix. But even the matrix is deposited under the influence of the corpuscles, for each of these has power to draw material from without into its interior, to assimilate it or

make it like itself (that is to say, convert it into its own substance and to cast off from its constitution the substances for which it has no further use); while many of them manufacture substances different from their own composition, and extrude them as soon as formed. Further, it is now universally allowed that all the nucleated corpuscles of our body are derived from pre-existing corpuscles. They have parentage and heredity just as much as separate organisms have. I need hardly say that single nucleated corpuscles of many forms occur as separate organisms. Indeed, we are so fond of illustrating the corpuscles of the tissues by reference to a particular set of small animals of the genus *amœba*, which throw out branches in different directions, and move about by means of those temporary limbs or *pseudopods*, that a corpuscle with similar powers of movement is often called an *amœboid* corpuscle. Not only so, but every living being, even the highest animal organism, in its earliest stage of existence, consists of a single corpuscle, which afterwards divides, so that, what was one corpuscle ultimately becomes two, and, by each of these dividing again in the same way, becomes the first parent of all the future corpuscles of the body. By such processes of multiplication of corpuscles all the textures are formed, and bone is no exception to the rule. Bone is one of the many textures which consist of corpuscle and matrix. There is a large group of tissues so constituted, often joined together under the name of connective or binding tissues. Typical connective tissue is that white substance which, for instance, in a raw beef-steak you can see joining together the fleshy parts or muscular fibres. It is called by various names in different circumstances according as it forms tendons, ligaments, or coverings of different densities; and bone is a specially modified form of this class of tissue, while gristle is another.

You will understand at once that the special peculiarity of bone which presents a difficulty to be got over in the way of nourishment and growth lies in the fact that it is so hard—very much harder than any of the other tissues. The difficulty may be well illustrated by reference to that texture from which the greater number of the bones in our body are formed—viz., cartilage, or more familiarly, gristle. You know that what afterwards constitutes a single bone is often, in the young animal, composed of separate parts. You may observe this in lamb for the table, or in so-called mutton: for you are aware that mutton is most frequently derived from anything but an adult specimen of the species. But

if you carry your observations further, and look at much younger bones, you will find you have large blocks of cartilage to deal with, and will often see bony tissue making its appearance in the heart of such blocks. Examined under the microscope, cartilage is seen to be made up of incapsuled corpuscles scattered through a stiff matrix. Thus, in this diagram, some little distance from the ossifying edge in the shaft of a young bone, still in great part cartilaginous, you will find the corpuscles scattered broadcast. But it happens that cartilage always grows more rapidly immediately previous to being converted into bone, as may be judged from the totally different arrangements of corpuscles met with as we approach the ossifying edge. There is a reason for this. Cartilage has no bloodvessels. There is nothing in it but what I have referred to—matrix and corpuscles. In bone there are abundant bloodvessels. Now, apparently, by the nearer approach of the bloodvessels in a growing bone, the cartilage-corpuscles find they are getting into a rich country full of sap, and they take to growing. That is the general explanation of what occurs. What is seen is, that a little nearer the ossifying edge than the scattered single corpuscles there are bunches of corpuscles which in section are lozenge-shaped. (Plate I., Fig. 1.) Each of these masses consists of the progeny of one such corpuscle as those above it. A little further down, each of these lozenge-shaped masses is replaced by a larger mass, and still going nearer the ossifying edge, you come upon larger and larger corpuscles arranged in groups which have changed their shape by stretching out into columns.

Now, consider what all this involves. Changes are taking place in the heart of the solid cartilage, in the region where the lozenge-shaped groups, of such a sort that where there was one little microscopic body in the middle of stiff matrix, there come afterwards to be two, with stiff matrix round about each. The same swelling of parts is going on in connection with the corpuscles nearer the ossifying edge, though the multiplication in that part has ceased for a time. All this means that undoubtedly the stiff substance already laid down is being pushed aside by new material, and that every particle of the cartilage is set in motion by the activities of the corpuscles that are contained within it; and in this way is illustrated a point which we have much more evidence of, that cartilage grows by interestitial expansion. Even in the heart of the mass expansion takes place freely. It looks at first sight

impossible that such a firm substance should be pushed aside by such minute structures as the corpuscles in its interior. But that there is such change actually going on is evidenced by microscopic appearances in every growing block.

Bone, however, is harder than cartilage. It has got a very large amount of mineral matter in its constitution—two-thirds of its weight being derived therefrom. If you take a mass of bone and steep it for months in muriatic acid you get rid of all the mineral matter; but neither the shape nor the microscopic structure is affected.

This [exhibiting a specimen] was a hard bone once, and retains its size and shape. You recognise in it a lumbar vertebra. But it is quite light; it can be squeezed together like a sponge, and resumes its size, because all the mineral matter with which the tissue was impregnated has been removed. So uniformly is the mineral matter distributed in the matrix of bone that it does not prevent the passage of the light through thin sections. Bone can be as easily examined by transmitted light as cartilage can be, and no evidence is afforded of the way in which it is deposited, even when we look with the highest powers of the microscope. Where cartilage is being converted into bone and the mineral matter is beginning to be deposited in it, the translucency is lost in the region of the columnar groups of corpuscles, where you find the gristle breaks away easily from the bone; and microscopists find this region difficult to deal with, until the mineral matter has been removed by means of acid. The reason of this is that the mineralised substance is in exceedingly minute patches, or granules, making, as one may say, so many spherical lenses of denser substance imbedded in a substance less dense. But when acid is added, the granules disappear and give place to uniform translucency, showing that they do not consist of pure mineral matter, but of mineralised animal matter, which, apart from its mineral impregnation, is exactly the same as its surroundings. Each is a little mass of bony substance, similar to that which afterwards forms the whole matrix of bone.

Now with regard to the ordinary nourishment of bone there is a difficulty as compared with cartilage. For although a few observers have brought under notice, over and over again, that there are complicated patterns in the matrix of cartilage, giving indications of channels more habitually made use of by the

currents of nourishment passing from one corpuscle to another than are the territories between, yet, notwithstanding this, it remains true, as is seen with ordinary methods, that there is unbroken continuity of matrix. But in bone the arrangement is different. The corpuscles are no longer incapsuled, but have numerous branches, and the substance in which they are imbedded is closely threaded with minute passages, by means of which the space containing one corpuscle communicates with others. (Fig. 2.) We call each space containing a bone-corpuscle, a *lacuna*, and the fine connecting canals, *canaliculi.* Sometimes the canaliculi are so wonderfully numerous as to be quite uncountable. They look like a rich head of hair combed out in different directions from each lacuna. It is liable to be taken for granted that they are formed round the branches of the corpuscles. Certainly some of them are so, but I think it must be an open question in the minds of most of us whether the whole of them are formed in that way. What is important to notice is that, owing to the exceeding density of the matrix in bone, it has become necessary that it should be broken up by a great number of perfectly definite canals, to allow sap to pass from corpuscle to corpuscle. There is thus an alteration in the character of the matrix as compared with that of cartilage, as well as an alteration in the character of the corpuscles, to allow of their ordinary nourishment; and the question with regard to the growth of bone which I specially had in my mind to speak on was, how this exceedingly dense texture was able to increase in size.

The most important points in answer to this question have been known to science for a very long time; in fact, John Hunter made numerous and conclusive experiments on the subject. Briefly, the difference between the growth of bone and the growth of cartilage, or any other tissue, may be put thus:—a mass of compact bone is not capable of being enlarged by multiplication of the corpuscles in its interior, nor by any forces of growth going on inside it; its increase in size is brought about altogether by additions at its circumference. I may perhaps best illustrate this by mentioning two experiments, both of which were made by Hunter. In one experiment he cut down on the humerus of a young pigeon. He passed a silver wire tightly round it, and put the little wound together, and the pigeon, none the worse, was, without the permission of any Secretary of State, allowed to live and enjoy life until it had grown, when, like most pigeons, it

came to an untimely end. When the humerus operated on came to be looked at, there was no silver ring to be seen till it was cut open, when the silver ring was found loose in the interior.

A bird's humerus is different from a mammal's, in respect that a mammal's humerus has a much greater thickness of bony substance, and is filled with marrow; while, in the bird, to make it lighter, the bone is exceedingly thin [exhibiting a specimen], almost like paper, and not only so, but it is filled with air, which it gets from the lungs by means of a special apparatus, and enters the humerus by a hole of very considerable size underneath the articular head. A bag continuous with the breathing apparatus pushes its way in at this aperture when the bird is young, and expands until it fills up the whole interior of the bone.

Now, to return to John Hunter's experiment. The circumstance that the silver ring was found lying loose inside shows that all the bone which had been originally grasped by it had disappeared. But while it was disappearing new bone was added in layers outside, and surrounded the ring. Here is a thigh bone of a rabbit in which, in like manner, new layers of bone have covered over a silver ligature. Thus we gain the information that a shafted bone increases in thickness by additional layers growing outside what has already been deposited; and further, that the marrow-cavity in a mammal, or the air-cavity in a bird, is formed by absorption of the bone previously existing. It might be thought that the walls of the young bone expanded as they grew bigger, got stretched out by some force so as to have a larger cavity in the interior than they had originally surrounded. But it has become evident that this is not the case. They disappear altogether, and new walls are formed.

So much for the growth in thickness. To understand growth in length it will be necessary to note that the shaft and the two extremities are ossified from separate centres, and remain long distinct. The shaft we call the *diaphysis*, the bony growths at the extremities, *epiphyses*. This arm-bone [exhibited] which I show you is long enough to belong to an adult, but it is not quite adult, for, as you see, the ossification has not been completed. There has been a very thin layer of cartilage between the shaft and each epiphysis, which has been removed in the process of preparation, so as to allow the three parts to fall separate. This is a condition which, as I mentioned, you have abundant means of studying in the lower animals, by using the opportunities which our habits of

diet give. Now, during the years in which the length was increasing, the lines of separation between the shaft and the epiphysis were gradually retreating from one another. The question comes to be—How was the shaft increased in length?

John Hunter's plan of trying to find the answer—a plan which has been repeated with modification by many others—was to insert shot at a measured distance in the bone of a growing animal. The wound was healed, and the animal kept alive until it became an adult, and it was found that though the bone had increased in length, the shot remained at exactly the same distance as when they were inserted. Thus it was proved that the shaft was increased in length by additions at the expense of the thin cartilaginous plates at its extremities; while there was no expansion in length of the bony matter already deposited, any more than in thickness. This doctrine has been denied even in our own time, but the denial has only brought other experimenters into the field, with the result that Hunter's views have been amply confirmed.

One experiment has been made which may interest you. The rabbit has in the fore-arm a radius and ulna similar to what we have. The lower end of the radius is thick, while the lower end of the ulna is slender, and both bones have an epiphysis at the the lower end. You will notice that if a shaft can only be elongated by additions where it is in contact with cartilage, its increase in length will cease when the cartilages are converted into bone. Founding on this, a German experimentalist, a good many years ago, made an experiment in the following way. He passed a needle into the cartilage which separated the lower end of a young rabbit's radius from the lower epiphysis, and so irritated it that it became converted into bone. But he left the ulna uninjured, with the result that after a time the fore-paw was completely turned inwards by the radius ceasing to elongate, while the continued elongation of the slender lower end of the ulna had power to push the outer side of the paw before it, distorting the limb and making the rabbit bandy-legged.

It is specially in compact bone that the peculiarities of growth which I have placed before you occur. It may be interesting for you to know how the ordinary process of nutrition goes on in that variety of bony tissue. If you look at a transverse section of a long bone, you find that the microscopic appearance is not uniform. The lacunæ and canaliculi are arranged in laminated fashion,

and especially you see concentric arrangements of laminæ round canals. There are such canals, containing bloodvessels, pervading the whole mass. They are called Haversian canals, after an old English physician, Clopton Havers, who was the first to detect their existence, but knew nothing of their contents. He described them as being for the animal spirits, and knew they were for the spirits because they were oily. The laminæ are disposed concentrically round spaces containing vessels, until at last the vessels are tightly surrounded by the innermost; and each such arrangement of laminæ round a vascular canal constitutes a Haversian system. Further, in young animals there are always, underneath the periosteum, regularly disposed lamellæ going round the whole bone. It was by these outer lamellæ that Hunter's pigeon's bones grew in girth; but if you had growth only of this description, you never would have the complex arrangement of concentric laminæ round Haversian canals, which form the main mass, and are packed together by portions of other concentric arrangements, whose rings are cut across by them. (Fig. 3.) For you not only see Haversian systems, in which lamellæ are arranged concentrically around a central canal containing one or more bloodvessels, but also series of laminæ abruptly cut across by more complete systems, and in many places not by any means parallel to the surface of the bone, or parallel to the marrow cavity in the interior of the bone, but forming portions of circles so small as to indicate that they themselves belong to pre-existing Haversian systems. You find, further, that you often meet with cavities of considerable size with only one or two lamellæ round them. These contain, among other things, corpuscles, sometimes called osteoblasts, by means of which new bone is formed from the soft tissues. These, in time, become completely imbedded in the bony matrix which they throw out.

The next set of corpuscles which will be developed on the osseous surface will get surrounded in the same fashion, till the concentric rings closely surround the bloodvessel. Such an open gap is what may be called a Haversian space, as distinguished from a Haversian canal, whose system of lamellæ is completed. There is another appearance regularly met with, consisting of hollows not surrounded by any laminæ arranged evenly round their circumference, but having ragged edges. On examining near the circumference of these cavities, there are always to be seen

enormous numbers of nucleated corpuscles, and very often five or six or more nuclei, in what appears to be one mass of protoplasm. These have been described as a separate order of giant corpuscles, having a special absorptive function, but, in reality, we have all along to deal with one race of corpuscles, which, in certain circumstances, take origin in soft tissue, and arrange themselves round surfaces of already deposited bone, to become themselves imbedded in osseous matrix; while at other times, being closely encompassed by bony matrix, they enter on a state of renewed activity, their nuclei multiplying, but the surroundings preventing the protoplasm breaking into separate masses, until it has made room by absorbing the bony matrix around.

The process of re-absorption of bone matrix may begin at a lacuna, or in a Haversian canal, or beneath the periosteum, or in the walls of the marrow cavity. But the Haversian systems are always produced by the eating away of bone which has been previously deposited, and the subsequent deposit of new bone, commencing in layers round the absorption-spaces, and proceeding concentrically till at last the spaces are completely filled.

Perhaps the most curious thing connected with bones is that this structural change is going on with a degree of rapidity which we do not yet clearly estimate, but is going on either more rapidly or more slowly all through life. It is only by this means we can account for the number of Haversian systems, perfect and partially obliterated, which we see brought together. The wasting of bones in old age is just performed by the same processes that have been going on through childhood and adolescence, and continued in the adult. The only difference is that absorption fails to be supplemented by redeposition. The special peculiarity running all through the history of bone, whether in growth or in old-age-wasting, or in the maintenance of the form in adult life, may be summed up in this:—that a mass of bone once laid down, however small it may be, is incapable even of allowing a single corpuscle to multiply into two or a larger number without there being at the same time a reabsorption of a certain amount of matrix; and this arises from that want of expansive power which Hunter's experiments proved as the characteristic feature of bone in the gross.

## Discussion.

Dr. Joseph Coats said—I think it would be a pity to spoil the impression left on our minds by Dr. Cleland's very clear

account of the process of the growth of the bones by any extended remarks; in fact, it would be impossible to criticise his paper—one can only have listened to it with the warmest appreciation. There is one thing which I may venture perhaps to add to what he has said. All these processes he has been describing so clearly to us are going on consistently with, and in the midst of, the functional activity of the bones. There is always a taking down and building up, and yet our bones are used, and used in young animals, I should say, much more vigorously than in adults. Throughout all the period of growth, involving these diverse processes of construction and reconstruction, the bones have to bear the continuous stress to which they, as the mechanical supports of the body, are exposed. In regard to the architecture of the bone, I was very much interested in reading a paper by Meyer of Zurich, in which he, with a series of most beautiful photographs representing sections of macerated bones, illustrated the internal structure of the bones. This showed that what we call the cancellated tissue at the ends of the long bones, and the whole of the interior of short bones, is not merely an indefinite mesh-work like a sponge, but a beautiful system of supporting columns for resisting the pressure to which the bone is exposed. By the merest accident I had an opportunity of seeing Professor Meyer's preparations while in Zurich, and was able to convince myself of the truth of his statements. The striking thing is, that while the bone is growing, and growing by this process of absorption and deposition, all this beautiful architecture is preserved. Meyer uses this fact as a very strong argument to show that the growth of bone is not by interstitial expansion, but by absorption and deposition; but his argument in that respect I need not go into.

The President—If no one has anything else to say, I shall make one or two brief observations. In the first place, we are much obliged to Dr. Cleland for coming here to-night and giving us this valuable communication. I know he has been making the subject of the growth of cartilage and bone a special study for a considerable time, and we are much favoured by receiving from him, at first hand, the results of his research—results which are all the more important from the fact that Dr. Cleland is a scientific worker who gives much interest, freshness, and originality to everything which he investigates. I have always been very much struck with the growth and development of bone. The story of

the growth of bone is one of the most interesting stories in physiological science. Dr. Cleland, at the outset of his remarks, referred to the fact that we know very little, indeed next to nothing, of the more intricate process by which the tissues are formed; and this is, no doubt, quite true. It is this region, however, that by and by we may hope to be able to penetrate. We have seen how these bone-corpuscles perform their marvellous work of building up the texture of bone, and of pulling it down again, but we must investigate, in the next place, how they perform this work. Each one is a mass of protoplasm, presenting, under the highest microscopic power, no special textural peculiarities that can explain its properties; and yet how marvellous it is that this little nucleated mass should have the power of separating from the blood the salts of lime that are dissolved in blood, and of precipitating these into its fibrous texture. And not only can it do this, but it deposits these little particles in a definite manner, and, after these have served their purpose, as Dr. Cleland has illustrated, the same kind of granular living masses pull it down. In other words, they have some peculiar power of redissolving the salts of lime, some of which are by no means very soluble, so that they are taken into the blood and carried away. There you have little bodies of granular living matter capable of performing this remarkable chemical process, and the physiology of the future will have to explain how these little masses of living matter can perform this work. The wider we take our survey of what is going on in nature, the more likely we are to get light upon a difficult problem like this. Bone is not the only substance in which we find living matter exercising powers over mineral matter. We know that in many of the lower forms of life, lower forms of invertebrates in the sea, for instance, such as sponges, foraminifera, and others, secrete earthy salts from the sea water, so as to form minute shells of exquisite forms, and in which not only salts of lime but even silica are deposited. There you have the process going on in the lower forms of life. Here in the bones of the higher animals you have a process of the same kind going on. I have no doubt that you will not readily forget—even those of you who have not studied this subject—Dr. Cleland's address. Many are apt to think of bone as a tissue in which active changes are not going on; at any rate, they do not think the changes are going on with great rapidity. But Dr. Cleland has demonstrated that, in early life especially, but also

throughout the whole of life, in every cubic inch of bone substance there are tens of thousands of minute corpuscles busily engaged in the work he has described. If you have not studied the subject you are apt to form an inadequate conception of the minute size of those organisms. The corpuscles are not larger than the 2000th or 2500th part of an inch, and even the so-called "giant cells" are very small things; yet it is by the incessant activity of these minute organisms that our bones grow. I was glad to hear Dr. Cleland express the view that our bodies, strangely complex as they are, represent a commonwealth of living things, each to a certain extent independent, and yet all working for the good of the whole. These are all engaged carrying on this work; but how little we do know of what guides them in their various movements, or the processes they carry on! In your name I return him our thanks.